No. 5,087,571 (hereafter "Leder") and also in view of Todaro *et al.*, (1963) J. Cell. Biol. 17:299-313 (hereafter "Todaro").

The only issue remaining in this application is whether the existence of Durbin's transgenic mice in combination with a general teaching that cell lines can be produced from transgenic mice (and immortalized) provides the motivation to prepare the claimed immortalized STAT1- deficient mammalian cell lines. Applicants respectfully submits that it does not.

Durbin teaches making transgenic mice completely deficient in the *Stat1* gene. The existence of these mice can not be a suggestion to make immortalized Stat1-deficient cell lines. In fact, the major focus of Durbin is to create *Stat1* $^{-/-}$ mice for studying the biological function of STAT1 *in vivo*. Durbin indicates these mice are for investigating STAT1 involvement in cytokine signaling and "to probe the roles of STAT1- linked pathways under physiologic settings and during development" (Durbin at Page 443, last paragraph of the right column). With this emphasis on discerning the role of STAT1 *in vivo,* Durbin teaches away from creation of an immortalized STAT1-/- cell line. Teaching away is a demonstration of lack of *prima facie* obviousness. *In re Dow Chemical Co.*, 837 F.2d 469 (Fed. Cir. 1988).

Moreover, Durbin fails to teach, suggest or even contemplate the need for an immortalized STAT1 mutant cell line since Durbin is expressly interested in the *in vivo* biology of Stat1. Durbin never suggests that its experiments would be better facilitated by having the use of such an immortalized STAT1- deficient cell line. In fact, Durbin's experiments did not need immortalized STAT1- deficient cell lines. Durbin neither discloses, teaches or suggests the immortalized STAT1- deficient cell lines of the

invention nor any utility for such immortalized cells such as hosts for producing viral stocks, for producing recombinant viral vectors, for detecting viruses and the like. As a result, one skilled in the art would not be motivated by Durbin to spend the time, money and effort making such an immortalized line.

In order for a claim to be rejected for obviousness in view of a reference under 35 U.S.C. § 103, the reference must teach or suggest each element of the claim. *See, Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 934 (Fed. Cir. 1990), *cert. denied*, 111 S.Ct. 296 (1990). Durbin wholly fails in this regard, so Durbin should be withdrawn as the primary reference.

The secondary references, Leder, Jallat and Todaro, do not ameliorate the deficiencies of Durbin. "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *In re Geiger,* 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed Cir. 1987). There is no doubt that Leder, Jallat and Todaro do not discuss or have any relationship whatsoever to Stat1 so that without Durbin providing motivation, which it does not, these references add nothing.

Applicants respectfully submit the Examiner is using improper hindsight to combine Durbin, Jallat, Leder and Todaro to allege that an immortalized STAT1-deficient cell line is obvious. "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to depreciate the claimed invention." *In re David H. Fine*, 837 F.2d 1071,1075 (Fed. Cir. 1988); 5 U.S.P.Q.2D (BNA) 1596 (Fed Cir. 1987). Such a combination of references from different fields of inquiry is improper without any motivation to combine those references. The Examiner must show that the

references make obvious the claimed invention not a general method of making immortalized cells.

Making immortalized cell lines is well known in the art. Just because a STAT1-deficient or any other transgenic mouse exists, that fact alone does not provide sufficient motivation to make an immortalized cell line from such a transgenic animal, absent some teaching or suggestion why such a cell line might be of interest.

Leder discloses the creation of a transgenic mouse containing an activated oncogene and a method for providing a cell culture from a transgenic animal in order to develop a genetically-sensitized model for assaying various compounds' carcinogenic properties *in vivo*. Jallat relates to creating a transgenic liver tumor cell line containing an exogenous DNA sequence for human factor IX and a second exogenous DNA sequence encoding either the SV40 virus T-antigen or the mouse c-myc gene. (Jallat at Column 3, Lines 22-27 and Lines 40-42; Column 4, Lines 15-19). Todaro discloses that spontaneously immortalized cell lines may be derived from normal Swiss mouse embryo cells (and possibly other cell types) after successive cell culture transfer and teaches that such an "established cell may have a bearing on the problem of carcinogenesis". (Todaro, page 299, lines 14-15).

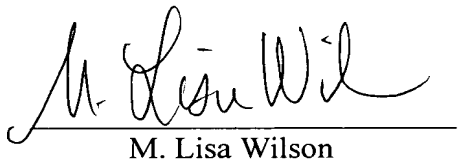
As a result, Leder, Jallat, and Todaro all teach how to make an immortalized cell line in fields of inquiry other than that of the present invention, yet all of these references fail to mention the *Stat1* gene, nor do they contemplate, teach or suggest any cell lines within the scope of the present invention. Thus no proper motivation exists for one skilled in the art to combine references from different fields of inquiry such as cancer research (Leder and Todaro) and recombinant protein production (Jallat) with Durbin

which relates to the study of "STAT1- linked pathways under physiologic settings and during development" (Durbin at Page 443). Applicants respectfully submit that to the combined teachings of Durbin, Jallat, Leder and Todaro to create the immortalized STAT1- deficient cells lines is nothing more than employing improper hindsight to reconstruct the claimed subject matter.

Accordingly, the rejection of claims 1-5 and 35-37 under 35 U.S.C. § 103 (a) over the cited combination of prior art is deemed obviated and withdrawal thereof is respectfully.

In view of the foregoing remarks it is firmly believed that the subject invention is in condition for allowance, which action is earnestly solicited. The Examiner is cordially invited to contact the undersign that would be helpful to advance prosecution of this application.

Respectfully submitted,



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